Simple and Condensed β-Lactams. Part 14.[1] Anomalous Behaviour of 1-(4-Methoxyphenyl)-4-(tetrazol-5-ylmethyl)azetidin-2-one Towards Cerium(IV) Ammonium Nitrate†

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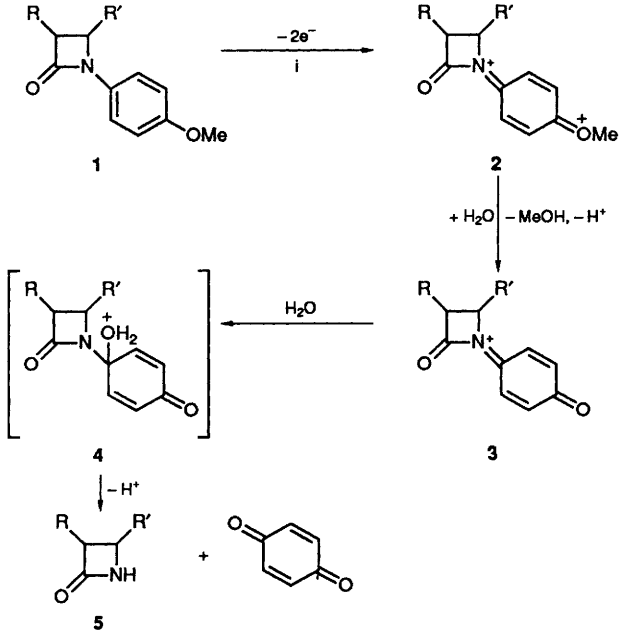
Treatment of 1-(4-methoxyphenyl)azetidin-2-one **7** with cerium(IV) ammonium nitrate (CAN) fails to yield the *N*-deprotected product **6**. Depending on the mode of work-up, *N*-substituted products **8–13** are obtained instead. The formation of these products may be rationalized by assuming interaction of the nucleophilic tetrazole and electrophilic quinone imine moieties of intermediate **21** to afford, after deprotonation, the spirocyclic quinone aminal **25**. The latter, in contrast to quinone imine derivatives of type **3**, is stable to hydrolysis under the conditions applied but reacts readily both with added sodium chloride and bromide as well as with reducing agents ($NaHSO_3$, I^-).

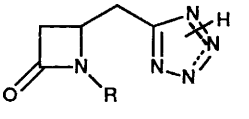
Treatment with cerium(IV) ammonium nitrate (CAN) is an established method for *N*-deprotection of *N*-(4-methoxyphenyl)azetidin-2-ones **1** in moderate to excellent yields.[2] The same transformation may also be brought about by anodic oxidation.[3] The generally accepted mechanism of both reactions involves initial oxidation of the starting β-lactam to dication **2**; this is followed by replacement of the $\overset{+}{O}Me$ group of **2** by an $\overset{+}{O}H$ group and proton loss to yield the quinone imine derivative **3** which is finally hydrolysed, probably *via* formation of intermediate **4**, to the *N*-deprotected β-lactam **5** and quinone[3] (Scheme 1). (Similar mechanisms have been postulated earlier for the oxidation of 1,4-dimethoxybenzene by CAN[4] and anodic oxidation of 4-alkoxyanilides.[5,6])



Scheme 1 Mechanism of *N*-deprotection of *N*-(4-methoxyphenyl)azetidin-2-ones by CAN or anodic oxidation. *Reagents:* i, CAN–MeCN–H_2O or anodic oxidation

† Based on parts of the Ph.D. Theses of E. K. and T. C., Technical University Budapest, 1989 and 1991

In connection with another research project, we were interested in studying the chemistry of 4-(tetrazol-5-ylmethyl)azetidin-2-one **6** which we wished to synthesize *via* its 1-(4-methoxyphenyl) derivative **7** by deprotection of the latter by treatment with CAN. To our surprise, the desired product was not formed; instead, azetidin-2-one **8**, containing a modified substituent attached to the ring nitrogen atom was obtained as the main product (see below) after suitable work-up (including treatment with aq. sodium chloride) of the reaction mixture. In order to study the structural requirements of this anomalous behaviour towards CAN, derivatives of compound **7** with methyl, benzyl and diphenylmethyl groups attached to the tetrazole ring (both isomers in all cases) were synthesized and their reactions with CAN studied.

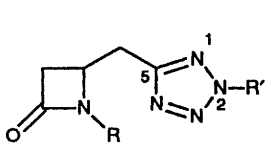


(±)-**6–14**

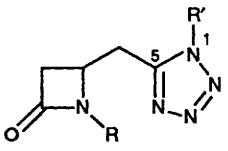
6 R = H
7 R = C_6H_4OMe–4
8 R = $C_6H_3Cl(OH)$–3,4
9 R = $C_6H_2Cl_2(OH)$–3,5,4
10 R = C_6H_4OH–4
11 R = $C_6H_3Br(OH)$–3,4
12 R = $C_6H_2Br_2(OH)$–3,6,4
13 R = $C_6H_2Br_2(OH)$–3,5,4
14 R = $CH_2C_6H_3(OMe)_2$–2,4

Reactions of 1-(4-*Methoxyphenyl*)-4-(*tetrazol-5-ylmethyl*)-*azetidin-2-ones* **7**, **15a–c** *and* **17c** *with CAN.*—While reaction of compound **7**, containing an *N*-unsubstituted tetrazole ring, with CAN took an anomalous course and did not lead to the *N*-deprotected product **6**, treatment of the *N*-substituted derivatives **15a–c** and **17c** did afford the expected deprotected compounds **16a–c** and **18c**, respectively, in moderate (non-optimized) yields. When, at a suitable point of the work-up procedure, the reaction mixture resulting from compound **7** was treated with aq. sodium chloride, compound **8** was obtained with its chlorine substituent originating from the sodium chloride added.

A dichotomy exists, therefore, in the reactions of azetidin-2-ones **7**, **15a–c** and **17c** with CAN. Since de(4-methoxyphenylation) of azetidin-2-ones **1** involves the intermediacy of type **3** quinone imine derivatives (Scheme 1), this dichotomy appears



15 R = C_6H_4OMe-4
16 R = H

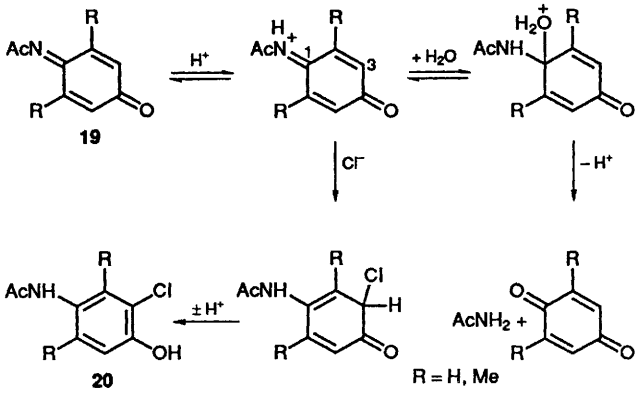


17 R = C_6H_4OMe-4
18 R = H

a R′ = Me
b R′ = $CHPh_2$
c R′ = CH_2Ph

to be related to certain observations of Novak *et al.*[7–9] These authors have noticed that acid catalysed hydrolysis of *N*-acetyl-*p*-benzoquinone imines **19** normally affords the expected *p*-benzoquinones and acetamide while, if the hydrolyses were conducted in the presence of added potassium chloride, 3-chloro-4-hydroxyacetanilides **20** became the main products. Taking into account *inter alia* the readiness of *p*-benzoquinone imines and of their *N*-protonated conjugate acids to react with nucleophiles, depending on the nature of the latter, at either the 1- or 3-position,[10,11] the mechanism shown in Scheme 2 has been suggested by Novak *et al.* for the acid catalysed hydrolysis of their quinone imines.[7–9]

In context with the observations of Novak *et al.* the non-



19 **20** R = H, Me

Scheme 2 Mechanism of acid catalysed hydrolysis of *N*-acetyl-*p*-benzoquinone imines in the presence and absence of added chloride ions[7–9]

formation of the *N*-deprotected product **6** from **7** by treatment with CAN could mean that intermediate **21** is stable in water, in contrast to all other related type **3** intermediates known up to now. Therefore, intermediate **21** remains unchanged until, during work-up, it is attacked by added chloride to yield ultimately compound **8**. In contrast, the related intermediates **22** in which the acidic tetrazole proton is replaced by methyl, diphenylmethyl or benzyl groups attached to N-1 or N-2 of the tetrazole ring do normally react with water, as shown by the formation of the deprotected products **16a–c** and **18c** respectively.

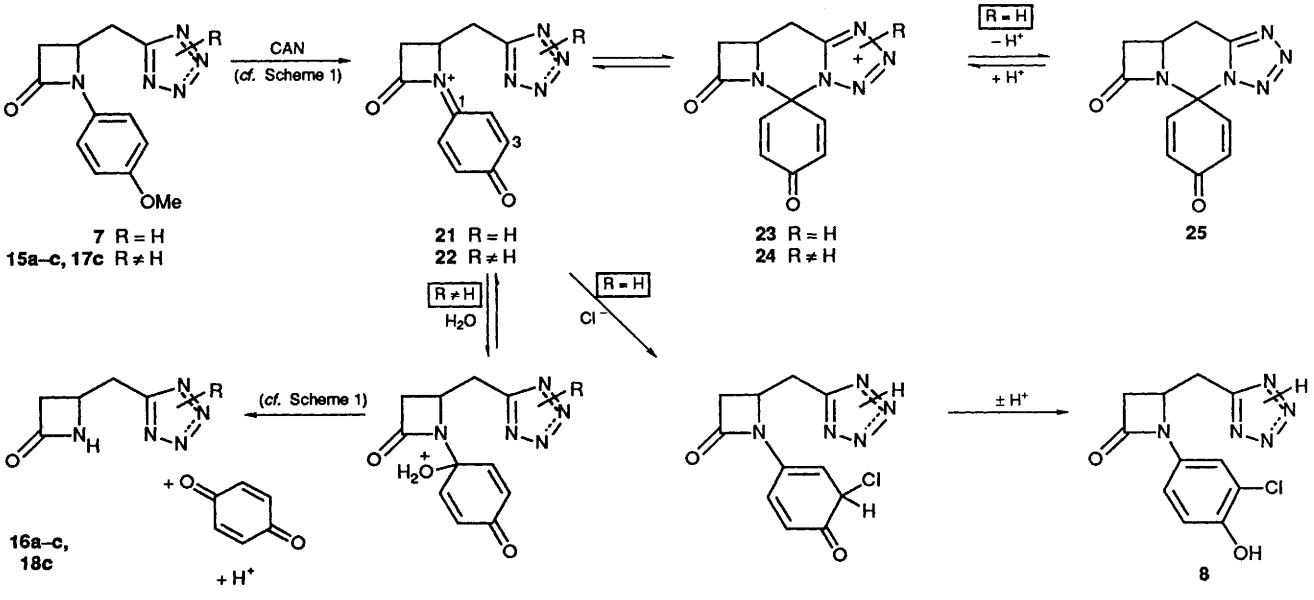
What is the reason for the widely divergent behaviour of these closely related intermediates?

We believe that reversible intramolecular nucleophilic attack at C-1 of the quinone iminium ring by a tetrazole nitrogen atom in a sterically favourable position may take place in both intermediates to afford spiranes **23** and **24**, respectively. In the case of the former (Scheme 3) the highly acidic tetrazolium hydrogen atom may be lost even in the acidic (pH ~ 2) reaction mixture with the result that a triple equilibrium (**21** ⇌ **23** ⇌ **25**) is set up. It is our view that the equilibrium is considerably shifted towards **25**, *i.e.* that intermediate **21** is effectively protected against intermolecular nucleophilic attack by a water molecule while intermediate **22** is not. Since attack at C-3 of the quinone iminium ring of intermediate **21** leads, in an irreversible manner, ultimately to compound **8**, this attack is not prohibited, in contrast to the attack of a water molecule at C-1.

Intermediate **25** is of the quinone aminal type. A related, non-spirocyclic derivative, compound **26**, is known from the literature; moreover, its mode of formation, *viz.* addition of aniline to the C=N bond of quinone imine **27**,[11] is analogous to the formation of compounds **23** and **24** suggested by us.

Further support for our view concerning the intermediacy of compound **21** and its stabilization by formation of an additional spirocyclic ring comes from the observations that (i) if the reaction mixture obtained on treatment of compound **7** with CAN is, after consumption of **7**, treated with aq. sodium bromide, the bromine analogue **11** of compound **8** is obtained among other products (see below), while (ii) similar treatment of the reaction mixture with sodium iodide or $NaHSO_3$ leads to the formation of the hydroxyphenyl derivative **10** (which is in agreement with the known ability of hydrogen iodide and $NaHSO_3$ to reduce quinone imines to aminophenols[12]).

Orientation in the addition of hydrogen chloride to com-



7 R = H
15a–c, 17c R ≠ H

21 R = H
22 R ≠ H

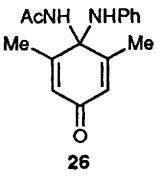
23 R = H
24 R ≠ H

25

16a–c, 18c

8

Scheme 3 Reaction of 1-(4-methoxyphenyl)-4-(tetrazol-5-ylmethyl)azetidin-2-ones with CAN. All compounds shown are racemic



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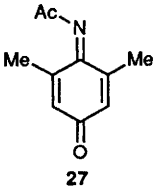

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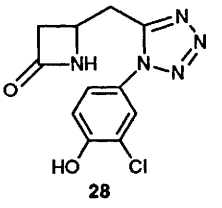

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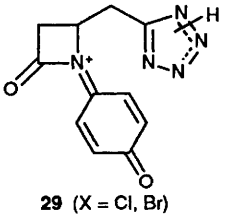


29 (X = Cl, Br)

pound **25** is determined by the site of initial protonation: the chlorohydroxyphenyl group will be attached in the product to a nitrogen atom of that hetero ring which had not been protonated initially. Since the tetrazole ring is more basic than the azetidinone moiety, compound **8** rather than the isomeric **28** is ultimately obtained. [Structure **28** is ruled out for the product by its IR spectrum which exhibits an intensive broad band (containing several local maxima) between 3100 and 2300 cm^{-1} characteristic of tetrazole derivatives bearing no *N*-substituent (*cf.* with the IR spectra of compounds **7** and **14**).]

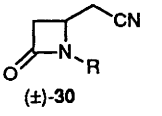
Both the EI and + FAB mass spectra of compound **8** revealed that it was contaminated with minor amounts of the symmetrical dichloro **9** and the non-chlorinated **10** analogues. Formation of the latter probably indicates that part of intermediate **21** ⇌ **23** ⇌ **25** has remained unchanged in the presence of NaCl and was subsequently reduced by $NaHSO_3$. An alternative pathway of formation of the non-chlorinated compound **10** (which would be analogous to its formation on treatment of the oxidation mixture with NaI), *viz.* that some of the intermediate **21** ⇌ **23** ⇌ **25** is reduced by NaCl, may not be ruled out at present.

When the oxidation mixture of compound **7** was treated with NaBr, work-up of the resulting semisolid products afforded crystalline mixtures of compounds **10**, **11** and **12** in one experiment, and of compounds **10**, **11** and **13** in another. (The difference in product composition is probably due to slight differences in the work-up procedures.) Since the amount of the non-halogenated compound was significant in both cases, the behaviour of equilibrium mixture **21** ⇌ **23** ⇌ **25** towards bromide anions appears to be intermediate between its behaviour towards chloride and iodide anions.

Formation of both symmetrical **9**, **13** and unsymmetrical **12** dihalogeno derivatives suggests that further halogenation of the monohalogeno derivatives could involve more than one distinct mechanism. One of these mechanisms appears to involve oxidation of the monohalogeno derivative by CAN to the corresponding halogenated quinone imine derivative **29**, followed by reaction of the latter with a halide anion (which would be similar to conversion **21** → → **8**, see Scheme 3). Support for this view comes from the observation that treatment of a mixture of compounds **10**, **11** and **13** successively with CAN and NaBr results in a substantial increase of the amount of the dibromo derivative **13** formed.

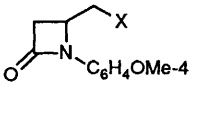
All attempts to isolate compound **25** from the reaction mixture obtained on treatment of compound **7** with CAN or to synthesize compound **25** by various alternative methods have so far failed.

Synthesis of 1-(4-*Methoxyphenyl*)- *and* 1-(2,4-*Dimethoxybenzyl*)-4-(*tetrazol-5-ylmethyl*)*azetidin-2-ones* **7** *and* **14*** *and of Derivatives of the Former Substituted at the Tetrazole Ring.*— The reaction of perchloro- and perfluoro-alkanenitriles (*i.e.* of electronegatively substituted alkanenitriles) with alkyl azides at 130–150 °C is known to afford 1,5-disubstituted tetrazoles in good yields.[13] The 4-(cyanomethyl)azetidin-2-one **30b**, synthesized earlier in this laboratory,[14] was therefore considered a convenient starting compound for the synthesis of type **14** compounds (carrying alkyl groups attached to their tetrazole rings) by applying the 1,3-dipolar cycloaddition methodology. However, compound **30b** did not react with butyl nor with octyl azide even after prolonged refluxing in either chloroform, benzene or toluene, and the starting materials were recovered unchanged. The 4-oxoazetidin-2-yl group is, apparently, not sufficiently electronegative to permit the desired cycloaddition to occur. Boron trifluoride–diethyl ether has been used successfully as a catalyst for the reaction of nitriles with hydrazoic acid.[15] However, addition of Lewis acids (boron trifluoride–



(±)-**30**

a R = C_6H_4OMe-4
b R = $CH_2C_6H_3(OMe)_2$-2,4



(±)-**31** X = OH
(±)-**32** X = O_3SMe
(±)-**33** X = I

diethyl ether, aluminium chloride) to mixtures of compound **30b** and butyl or octyl azide in either of the solvents mentioned failed to bring about the desired cycloaddition and led to profound decomposition. This parallels similar observations by Carpenter.[13]

Ionic azides do cycloadd to nitriles more readily than their covalent counterparts.[15,16] Therefore reaction of compound **30b** with sodium azide was next attempted. Heating the reactants in DMF (dimethylformamide) or DMSO (dimethyl sulfoxide) in the presence of anilinium chloride as a phase-transfer and acid catalyst to 130 °C (these are the conditions recommended by Finnegan *et al.*[15]) led to profound decomposition, and not even traces of the desired product **14** were obtained. When, however, *N*-methylpyrrolidin-2-one was used as the solvent and triethylammonium chloride as the catalyst (*cf.* ref. 16) compound **14** was obtained in 54% yield. The same compound was obtained, in considerably lower yield (16%) in *N*,*N*-dimethylacetamide solvent. Compound **7** was similarly obtained from **30a** (itself synthesized in three steps starting with the hydroxymethyl derivative **31**[17]) in 55% yield in *N*-methylpyrrolidin-2-one solvent. Compound **30a** was converted into compound **7** in considerably improved yield (82%) when the method of Arnold and Thatcher[18] was applied to this particular case, *i.e.* when aluminium azide (generated *in situ* from sodium azide and anhydrous aluminium chloride) rather than sodium azide was used as the source of three contiguous nitrogen atoms of the tetrazole ring to be constructed.

Treatment of compound **7** with diazomethane in dioxane led to a mixture of two isomeric *N*-methyl derivatives **15a** (81%) and **17a** (18%). Similarly obtained were the two isomeric *N*-(diphenylmethyl) derivatives **15b** (79%) and **17b** (20%) by treating compound **7** with diphenyldiazomethane. Finally, reaction of compound **7** with benzyl iodide in ethanol in the presence of sodium ethoxide afforded the two isomeric *N*-benzyl derivatives **15c** (44%) and **17c** (35%). The isomers were separated in all three cases by column chromatography. The

* Potential methods of synthesis of compound **7** were first tested by applying them to the synthesis of the *N*-(2,4-dimethoxybenzyl) analogue **14** used as a model compound.

structures of the isomeric *N*-methyl and *N*-benzyl derivatives were initially derived by evaluating differences in the multiplicities and chemical shifts of the signals of the tetrazole *N*-substituents. Thus, while both signals of the benzyl group of the less polar isomer are singlets (δ_H 5.7, 2 H; 7.35, 5 H) the more polar isomer exhibits an AB signal (δ_H 5.38 + 5.40, J_{gem} 15 Hz, 2 H) and a multiplet (δ_H 7.0–7.45, 5 H). This demonstrates that rotation of the benzyl group about the N–C bond is free in the former compound, while it is hindered in the latter, and suggests that the benzyl group in the less polar isomer is attached to N-2 of the tetrazole ring but to N-1 in the more polar isomer. Thus, the methylene signal of the benzyl group of the less polar isomer **15c** appears at lower field (δ_H 5.7) than that of the more polar isomer **17c** (δ_H 5.4). A similar correlation exists for the *N*-methyl signals of the two *N*-methyl derivatives: the *N*-methyl signal of the less polar isomer is found at lower field (δ_H 4.32 s; $CDCl_3$) than that of the more polar one (δ_H 3.90 s; [$^2H_6$]-DMSO + $CDCl_3$). This suggests that, here again, the less polar isomer is the N-2 substituted **15a** and the more polar one the N-1 substituted derivative **17a**. These structural assignments were corroborated by NOE studies. Selective irradiation of the methylene proton signal of the benzyl group of the more polar isomer **17c** caused the intensity of the signal of the methylene group attached to C-4 to increase, demonstrating thereby that the two methylene groups of this isomer are indeed in the vicinity of each other. Similarly, selective irradiation of the methyl signal of the more polar isomer **17a** caused the intensity of the signal of one proton * of the methylene group attached to C-4 to increase, demonstrating again that these groups in the more polar isomer are in the vicinity of each other. Finally, the ^1H NMR spectra of the less and more polar *N*-diphenylmethyl derivatives correlated very well with the spectra of the less and more polar *N*-benzyl derivatives, respectively (all spectra taken in $CDCl_3$). On this basis the less polar *N*-diphenylmethyl derivative was assigned structure **15b** and the more polar isomer structure **17b**.

Experimental

Separations of product mixtures by column chromatography were carried out at normal or reduced (10–25 kPa) pressure using Kieselgel 60 (Merck) as the adsorbent. For preparative TLC separations 20 × 20 cm glass plates coated with Kieselgel $PF_{254+366}$ (Merck; thickness of adsorbent layer 1.5 mm) were used. The purity of the products was checked and their R_f values were determined on DC-Alufolien 60 F_{254} (Merck); the individual compounds were detected by UV irradiation or using iodine, 5% ethanolic molybdo-, or tungsto-phosphoric acids as the reagents.

Melting points were determined in glass capillaries and are uncorrected. IR spectra were recorded on a Specord-75 (Zeiss, JENA) spectrometer. ^1H and ^{13}C NMR spectra were obtained with Varian XL-100 and XL-400 spectrometers in $CDCl_3$ solutions at *ca.* 50 °C, unless otherwise stated, and using tetramethylsilane as the internal reference compound; *J* values are given in Hz. EI mass spectra were obtained at 70 eV with an AEI MS 902 instrument equipped with a direct insertion system. Positive ion FAB mass spectra were obtained with a VG ZAB-2SEQ spectrometer with reversed geometry and equipped with a caesium gun; glycerol and *m*-nitrobenzyl alcohol were used as the matrix solvents.

Reaction of 1-(4-*Methoxyphenyl*)-4-(*tetrazol*-5-*ylmethyl*)-*azetidin*-2-*ones* **15a–c** *and* **17c** *with CAN: General Procedure*.†—An aqueous solution (15 cm^3) of CAN (1.65 g, 3 mmol) was added dropwise to a solution of the starting azetidinone (1 mmol) in acetonitrile (15 cm^3) at −5 °C. Stirring was continued for 1 h at this temperature. The mixture was made slightly alkaline (pH 8) by adding saturated aq. Na_2CO_3, the resulting precipitate was filtered off and washed with five portions (2 × 10 and 3 × 5 cm^3) of ethyl acetate which were subsequently used for extraction of the original aqueous filtrate. The combined organic phases were successively washed with 10% aq. $NaHSO_3$‡ (3 × 5 cm^3) and 5% aq. $NaHCO_3$ (3 × 5 cm^3) and brine (3 × 5 cm^3), dried ($MgSO_4$) and worked up by column chromatography (CH_2Cl_2–acetone, 7:1).

The following products were obtained. 4-(2-*Methyltetrazol*-5-*ylmethyl*)*azetidin*-2-*one* (**16a**). From compound **15a** (0.7 g, 2.55 mmol) (90 mg (21%)) as an oil (Found: C, 42.95; H, 5.55; N, 14.65. $C_6H_9N_5O$ requires C, 43.05; H, 5.4; N, 14.85%); ν_{max}(film)/cm^{-1} 3300 and 1760; δ_H 2.82 + 3.15 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, $^4J_{NH}$ 1.5 and 2.0, 3-H_2), 3.18 + 3.25 (*ABX*, J_{gem} 15.0, J_{vic} 7.2 and 5.8, 4-CH_2), 4.05 (m, 4-H), 4.31 (s, *N*-Me) and 6.45 (br s, NH).

4-(2-*Diphenylmethyltetrazol*-5-*ylmethyl*)*azetidin*-2-*one* **16b**. From compound **15b** (3.2 g, 7.5 mmol) 1.9 g (79%) as an oil (Found: C, 67.85; H, 5.45; N, 22.05. $C_{18}H_{17}N_5O$ requires C, 67.65; H, 5.3; N, 21.9%); ν_{max}(film)/cm^{-1} 3250 and 1750; δ_H 2.78 + 3.11 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, $^4J_{NH}$ 1.5 and 2.0, 3-H_2), 3.18 + 3.26 (*ABX*, J_{gem} 15.0, J_{vic} 7.3 and 5.5, 4-CH_2), 4.03 (m, 4-H), 6.2 (br s, NH) and 7.05–7.55 (2 × Ph + Ph_2CH).

4-(2-*Benzyltetrazol*-5-*ylmethyl*)*azetidin*-2-*one* **16c**. From compound **15c** (0.5 g, 1.4 mmol) 0.22 g (63%) as an oil (Found: C, 60.0; H, 5.3; N, 28.7. $C_{12}H_{13}N_5O$ requires C, 59.25; H, 5.35; N, 28.8%); ν_{max}(film)/cm^{-1} 3300 and 1750; δ_H 2.79 + 3.13 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, $^4J_{NH}$ 1.5 and 2.0, 3-H_2), 3.15 + 3.25 (*ABX*, J_{gem} 15.0, J_{vic} 7.5 and 5.5, 4-CH_2), 4.04 (m, 4-H), 5.73 (s, CH_2Ph), 6.25 (br s, NH) and 7.37 (s, Ph).

4-(1-*Benzyltetrazol*-5-*ylmethyl*)*azetidin*-2-*one* **18c**. From **17c** (455 mg, 1.3 mmol) 125 mg (40%) as an oil (Found: C, 59.6; H, 5.4; N, 29.0. $C_{12}H_{13}N_5O$ requires C, 59.25; H, 5.35; N, 28.8%); ν_{max}(film)/cm^{-1} 3300 and 1750; δ_H 2.65 + 3.10 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, $^4J_{NH}$ 1.0 and 2.2, 3-H_2), 2.99 + 3.02 (*ABX*, J_{gem} 15.5, J_{vic} 7.5 and 5.5, 4-CH_2), 4.05 (m, 4-H), 5.65 (s, CH_2Ph), 6.5 (br s, NH) and 7.1–7.5 (Ph).

Reactions of 1-(4-*Methoxyphenyl*)-4-(*tetrazol*-5-*ylmethyl*)-*azetidin*-2-*one* **7** *with CAN and Sodium Halides*.—(*a*) An aqueous solution (70 cm^3) of CAN (8.3 g, 15.0 mmol) was added dropwise with vigorous stirring and ice–water cooling to a mixture of compound **7** (1.3 g, 5.0 mmol), acetonitrile (52 cm^3) and dioxane (10 cm^3). The mixture was stirred for an additional 1 h at this temperature and diluted with water (90 cm^3). Crystalline NaCl was added until the aqueous phase became saturated with NaCl. The two phases were separated and the aqueous phase was extracted with ethyl acetate (3 × 70 cm^3). The combined organic solutions were washed with 10% aq. $NaHSO_3$ (3 × 50 cm^3), dried ($MgSO_4$) and evaporated to dryness at reduced pressure. The residue was recrystallized from methanol to yield 1-(3-*chloro*-4-*hydroxyphenyl*)-4-(*tetrazol*-5-*ylmethyl*)*azetidin*-2-*one* **8** [1.1 g, 79%; m.p. 233–235 °C; R_f 0.15 (CH_2Cl_2–MeOH, 8:2) (Found: C, 47.15; H, 3.75; Cl, 12.0; N, 24.35. $C_{11}H_{10}ClN_5O_2$ requires C, 47.25; H, 3.6; Cl, 12.7; N, 25.05%); ν_{max}(KBr)/cm^{-1} 3500, 3100–2300 (br, with several local maxima) and 1720; δ_H(400 MHz; $CDCl_3$ + [$^2H_6$]-DMSO) 2.99 + 3.24 (*ABX* J_{gem} 15.3, J_{vic} 2.4 and 5.3, 3-H_2), 3.22 + 3.64 (*ABX*, J_{gem} 15.1, J_{vic} 8.7 and 4.0, CH_2-Tet), 4.48 (dddd, *J* 2.4, 5.3, 8.7 and 4.0, 4-H), 6.95 (d, *J* 8.7, 5-H, phenyl ring), 7.07 (dd, *J* 8.7 and 2.6, 6-H, phenyl ring), 7.36 (d, *J* 2.6, 2-H, phenyl ring) and

* Since the signal of the second proton is partly blurred by the DMSO signal, the change of its intensity could not be observed unequivocally.

† Given for the reaction of 1 mmol of substrate.

‡ The dark colour of the reaction mixtures was thereby removed.

9.30 (br s, OH + NH); δ_C($CDCl_3$ + [$^2H_6$]-DMSO) 26.32 (CH_2-Tet), 42.13 (C-3), 48.72 (C-4), 116.40 (C-6, phenyl ring), 116.76 (C-5, phenyl ring), 118.51 (C-2, phenyl ring), 120.19 (C-3, phenyl ring), 129.54 (C-1, phenyl ring), 149.46 (C-4, phenyl ring), 152.60 (Tet) and 162.80 (C-2); weak signals corresponding to contaminants **9** and **10** were also observed and assigned as follows: **9** (~5%) δ_H 3.01 + 3.27 (*ABX* J_{gem} 15.2, J_{vic} 2.4 and 5.3, 3-H_2), 3.25 + 3.65 (*AB*X, 4-CH_2) 7.30 (s, 2- and 6-H, dichlorohydroxyphenyl group); **10** (~2%) δ_H 2.96 (one half of an *ABX* spectrum, 3-H_2), 3.19 (one half of an *ABX* spectrum, 4-CH_2), 6.80 + 7.18 (AA′BB′, 4-hydroxyphenyl group); the other signals of these contaminants were blurred by the signals of the main component and could not be assigned; FAB MS (glycerol): MH^+ *m/z* 280, MNa^+ 302; EI MS (70 eV, 170 °C) *m/z* (I%) 315 (0.7, i), 313 (1.2, $M_3^{\bullet+}$), 281 (19, i), 279 (59, $M_2^{\bullet+}$), 271 (0.5, [$M_3^{\bullet+}$ − CH_2CO]), 245 (5, $M_1^{\bullet+}$), 239 (10, i), 237 (33, [$M_2^{\bullet+}$ − CH_2CO]), 196 (9), 194 (10), 192 (10), 174 (8), 173 (19), 172 (23), 171 (21, i), 169 (65, [$M_2^{\bullet+}$ − $C_4H_6N_4$]), 156 (34, i), 154 (100, $Cl(HO)C_6H_3\overset{+}{N}{\equiv}CH$), 145 (28, i), 143 (75, $Cl(OH)C_6H_3\overset{+}{N}H_2$), 141 (18), 133 (27), 129 (8, i), 127 (24, $Cl(HO)C_6H_3^+$), 101 (9, i), 99 (26, $ClC_5H_4^+$), 38 (16, i) and 36 (50, HCl); $M_1^{\bullet+}$, $M_2^{\bullet+}$ and $M_3^{\bullet+}$ are the molecular ions of compounds **10**, **8** and **9**, respectively, their relative amounts in the product, as deduced from the relative intensities of the molecular bundles, being 2:92:6, in excellent agreement with the relative amounts of these compounds deduced from the ^1H NMR spectrum; i indicates isotope peaks.

(*b*) An aqueous solution (30 cm^3) of CAN (4.05 g, 7.4 mmol) was added dropwise with vigorous stirring to a suspension of compound **7** (0.64 g, 2.47 mmol) in acetonitrile (64 cm^3) between −10 and 0 °C. Stirring was continued for 2 h at this temperature and the resulting emulsion divided into three equal parts.

One third of the reaction mixture was treated with crystalline NaCl (b_1) as in (*a*) and another third was treated similarly with crystalline NaBr (b_2). Further work-up was identical in both cases. Thus, the resulting two phases were separated and the aqueous phase extracted with ethyl acetate (5 × 25 cm^3). The combined organic solutions were washed with 10% aq. $NaHSO_3$ (3 × 25 cm^3), dried ($MgSO_4$) and evaporated to dryness at reduced pressure. The residue was taken up in a small amount of methanol and the light yellow crystalline products filtered off.

The product from b_1 (70 mg, 30.5%; m.p. 243–244 °C) was shown by its ^1H NMR spectrum [which was practically identical with that of the sample obtained as described in (*a*)] to be almost pure **8**. The product from b_2 [46 mg, 20%; m.p. 251–253 °C; ν_{max}(KBr)/cm^{-1} 3500, 3150–2300 and 1720] was shown by its ^1H NMR spectrum to be a mixture of compounds **10**, **11** and **12**, **10** being the most abundant and **12** only a minor component. δ_H($CDCl_3$ + [$^2H_6$]DMSO; 400 MHz; the chemical shifts of the individual components were extracted from the spectrum of the mixture) **10**: δ_H 2.94 + 3.21 (*ABX*, J_{gem} 14.9, J_{vic} 2.4 and 5.2, 3-H_2), 3.22 + 3.62 (*ABX*, J_{gem} 15.0, J_{vic} 8.5 and 3.5, 4-CH_2), 4.48 (dddd, *J* 2.4, 5.2, 8.5 and 3.5, 4-H), 6.77 + 7.17 (AA′BB′, 4-hydroxyphenyl group), 9.2 (br s, OH + NH; collapsed with the corresponding signals of the other two components); **11**: 2.97 + 3.24 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.3, 3-H_2), 3.25 + 3.61 (*ABX*, J_{gem} 15.0, J_{vic} 8.3 and 3.5, 4-CH_2), 4.50 (dddd, *J* 2.5, 5.3, 8.3 and 3.5, 4-H), 6.93 (d, *J* 8.7, 5-H, aryl group), 7.11 (dd, *J* 8.7 and 2.5, 6-H, aryl group) and 7.52 (d, *J* 2.5, 2-H, aryl group); **12**: 3.10 + 3.48 (*ABX*, J_{gem} 15.2, J_{vic} 2.6 and 5.2, 3-H_2), 3.27 + 3.97 (*ABX*, J_{gem} 15.2, J_{vic} 10.5 and 1.8, 4-CH_2), 4.10 (dddd, *J* 2.6, 5.2, 10.5 and 1.8, 4-H) and 7.67 + 7.53 (2 s, 2 ArH); EI MS (70 eV, 170 °C) *m/z* (I%) 405 (0.7, i), 403 (1.2, i), 401 (0.6, $M_3^{\bullet+}$), 325 (18, i), 323 (19, $M_2^{\bullet+}$), 283 (8, i), 281 (9, [$M_2^{\bullet+}$ − CH_2CO]), 245 (100, $M_1^{\bullet+}$), 215 (9, i), 213 (9, [$M_2^{\bullet+}$ − $C_4H_6N_4$]), 203 (33, [$M_1^{\bullet+}$ − CH_2CO]), 200 (12, i), 198 (11, Br-(HO)$C_6H_3\overset{+}{N}{\equiv}CH$), 189 (37, i), 187 [39; Br(HO)$C_6H_3\overset{+}{N}H_2$]), 135 (67, [$M_1^{\bullet+}$ − $C_4H_6N_4$]), 120 (78, $HOC_6H_4\overset{+}{N}{\equiv}CH$), 109 (42, $HOC_6H_4NH_2^+$), 107 (18), 93 (19, $HOC_6H_4^+$); $M_1^{\bullet+}$, $M_2^{\bullet+}$ and $M_3^{\bullet+}$ denote the molecular ions of compounds **10**, **11** and **12**, respectively.

(*c*) Compound **7** (0.64 g, 2.47 mmol) was oxidized as described in (*b*). The resulting mixture (which, according to TLC, contained no unchanged starting compound **7**) was saturated with crystalline NaBr, stirred for 0.5 h at ~0 °C and extracted with EtOAc (5 × 30 cm^3). The organic phases were combined, crystalline $MgSO_4$ and $Na_2S_2O_5$ were added and the mixture stirred for ~15 min. The salts were filtered off and the filtrate was evaporated to dryness at reduced pressure. The residue was triturated with a small amount of methanol to give a faint yellow crystalline product (0.59 g, 80%), m.p. 228 °C, which was shown by its ^1H NMR spectrum to be a mixture of compounds **10**, **11** and **13** in an approximate molar ratio of 35:63:2. The observed ^1H NMR spectrum (400 MHz; $CDCl_3$ + [$^2H_6$]DMSO) was a weighted average of the spectra of the individual components. For the spectra of compounds **10** and **11**, see above. For the minor component **13** only the signals of the aryl protons (7.51; s, 2-H + 6-H) could be identified which, however, was sufficient for proof of the symmetrical substitution pattern of the aryl group, *i.e.* of structure **13**.

(*d*) Further oxidation of the mixture obtained as described in (*c*). An acetonitrile (40 cm^3) solution of the mixture [0.39 g; consisting of compounds **10** (0.46 mmol), **11** (0.82 mmol) and **13** (0.03 mmol); total 1.31 mmol] was subjected to successive treatment with aqueous (18 cm^3) CAN (2.25 g, 4.1 mmol) solution and crystalline NaBr as described in (*c*). The residue (0.3 g), obtained on evaporation of the EtOAc solution under reduced pressure, failed to crystallize and was therefore worked up by TLC (Kieselgel PF_{254}; CH_2Cl_2–MeOH, 2:1). One of the main fractions (which, too, failed to crystallize; 0.18 g) was shown by its ^1H NMR spectrum to be a mixture of compounds **10**, **11**, **13** and of an unidentified substance containing a tetrasubstituted *N*-aryl group with its two hydrogen atoms in *meta* position relative to each other (δ_H 6.75 and 6.95, 2 × s, *J* 2.8) in an approximate molar ratio of 21:34:42:3. Hence the amounts of compounds **10**, **11** and **13** in this fraction were 0.11, 0.19 and 0.23 mmol, respectively, *i.e.* the amount of the symmetrical dibromo derivative **13** has considerably increased. In the ^1H NMR spectrum of the mixture the signals of the saturated protons of the individual components were mutually blurred and, therefore, less sharp. The signals of the aromatic protons, however, were sharp [δ_H($CDCl_3$ + [$^2H_6$]DMSO) **10** 6.80 + 7.23 (AA′BB′, *J* 8.6); **11** 6.99 (d, *J* 8.5, 5-H), 7.09 (dd, *J* 8.5 and 2.5, 6-H), 7.63 (d, *J* 2.5, 2-H); **13** 7.51 (s, 2-H + 6-H)] and permitted identification of the individual components and estimation of their relative amounts. The EI MS (70 eV, 170 °C) of the product displayed characteristic and abundant peaks corresponding to compounds **11** and **13** and weak peaks corresponding to compound **10** such as $M_i^{\bullet+}$, ($M_i^{\bullet+}$ − 110), ($M_i^{\bullet+}$ − 125) and ($M_i^{\bullet+}$ − 136) with i = 1, 2 and 3, and $M_1^{\bullet+}$, $M_2^{\bullet+}$ and $M_3^{\bullet+}$ being the molecular ions of compounds **10**, **11** and **13**, respectively. From high resolution measurements exact masses were obtained for M_3 and M_2. Found: M_3 = 400.914, M_2 = 323.003; $C_{11}H_9{}^{79}Br_2N_5O_2$ and $C_{11}H_{10}{}^{79}BrN_5O_2$ require 400.9124 and 323.0018, respectively.

(*e*) Compound **7** (0.64 g, 2.47 mmol) was oxidized as described in (*b*). The resulting mixture was saturated with crystalline NaI and then worked up as described in (*c*) to afford the reduced product **10** (0.28 g, 44%; m.p. 261–262 °C) which, according to its ^1H NMR spectrum [which was almost identical with that of the main component of the mixture obtained as described in (b_1)] was ~95% pure. The non-identified but, according to its ^1H NMR spectrum [δ_H($CDCl_3$ + [$^2H_6$]DMSO) 2.93 + 3.30 (*ABX*, J_{gem} 14.8, J_{vic} 2.4 and 5.3,

3-H_2), 3.10 (d, J 4.5, 4-CH_2), 4.39 (tdd, J_{vic} 4.5, 2.4 and 5.3, 4-H), 6.78 + 7.21 (AA′BB′, J 8.7, 4 × ArH, 4-hydroxyphenyl group)] (extracted from the spectrum of the mixture), structurally closely related contaminant (~5%) appears to differ from the main component by having the 4-tetrazol-5-ylmethyl) substituent replaced by a 4-(X-methyl) group. FAB MS (matrix *m*-nitrobenzyl alcohol) *m/z* (I%) 246 (70; $MH^{+\bullet}$), 245 (100, $M^{+\bullet}$); EI MS (70 eV, 170 °C) *m/z* (I%) 285 (2.5, impurity), 245 (78, $M^{+\bullet}$), 203 (25, $M^{+\bullet} - CH_2CO$), 202 (29, 203 − H), 135 (58, $M^{+\bullet} - C_4H_6N_4$), 120 (100, 203 − $C_2H_3N_4$), 109 (68, 203 − $C_3H_2N_4$), 93 (21, $C_6H_4OH^+$) (Found: M, 245.0905. $C_{11}H_{11}N_5O_2$ requires *M*, 245.0913).

1-(4-*Hydroxyphenyl*)-4-(*tetrazol*-5-*ylmethyl*)*azetidin*-2-*one* **10**.—An aqueous (85 cm^3) solution of CAN (8.5 g, 15.4 mmol) was added dropwise to a solution of compound **7** (2.0 g, 7.7 mmol) in acetonitrile (200 cm^3) at −5 °C. Stirring was continued for 1 h at this temperature. Crystalline $Na_2S_2O_5$ was added until the aqueous phase became saturated. The latter was separated and extracted with ethyl acetate (5 × 50 cm^3). The combined organic solutions were dried ($MgSO_4$) and evaporated to dryness at reduced pressure. The residue was triturated with acetone, filtered off and washed with a small amount of acetone to afford the title compound [1.75 g, 92%; m.p. 254 °C; ν_{max}(KBr)/cm^{-1} 3500–3150, 3100–2400, 1700 and 820]. The ^1H NMR spectrum was practically identical with that of the main component of the mixture obtained by CAN oxidation and subsequent NaBr or NaI treatment of compound **7**, see above.

(±)-4-(*Methylsulfonylmethyl*)-1-(4-*methoxyphenyl*)*azetidin*-2-*one* **32**.—Methanesulfonyl chloride (14.1 g, 123 mmol) was added dropwise with vigorous stirring and ice–water cooling within 10 min to a solution of compound **31**[17] (20.1 g, 97 mmol) in pyridine (68 cm^3). The mixture was stirred for 3 h at room temperature and evaporated to dryness at reduced pressure. The dry residue was taken up in CH_2Cl_2 (100 cm^3), the solution washed with 2 mol dm^{-3} aq. HCl (2 × 50 cm^3) and water (2 × 50 cm^3), dried ($MgSO_4$), and evaporated to dryness. The residue was crystallized from methanol (1.5 parts) to afford the title compound (23.9 g, 85%), m.p. 102 °C, R_f 0.68 (benzene–acetone, 6:4) (Found: C, 50.7; H, 5.4; N, 4.95; S, 11.2. $C_{12}H_{15}NO_5S$ requires C, 50.51; H, 5.30; N, 4.91; S, 11.24%) ν_{max}(KBr)/cm^{-1} 1740, 1510, 1380, 1180 and 830; δ_H 2.92 (s, O_3SMe), 2.98 + 3.23 (*AB*X, J_{gem} 15.0, J_{vic} 2.5 and 5.3, 3-H_2), 3.79 (s, OMe), 4.38 (m, 4-H), 4.51 (m, CH_2O_3SMe) and 6.90 + 7.35 (AA′BB′, J 9.0, 4 × ArH).

(±)-4-*Iodomethyl*-1-(4-*methoxyphenyl*)*azetidin*-2-*one* **33**.—A mixture of compound **32** (19.6 g, 69 mmol), anhydrous acetone (150 cm^3), and freshly dried sodium iodide (45 g, 0.3 mol) was refluxed for 12 h and evaporated to dryness at reduced pressure. The residue was triturated with water (50 cm^3) and extracted with CH_2Cl_2 (2 × 30 and 1 × 15 cm^3). The combined CH_2Cl_2 solutions were dried ($MgSO_4$) and evaporated to dryness to afford a solid residue (21 g) from which the title compound [19.4 g, 89%; m.p. 94–95 °C; R_f 0.74 (benzene–acetone, 4:1)] was obtained by crystallization from ethanol (60 cm^3) (Found: C, 41.55; H, 3.85; I, 40.05; N, 4.2. $C_{11}H_{12}INO_2$ requires C, 41.66; H, 3.81; I, 40.02; N, 4.42%) ν_{max}(KBr)/cm^{-1} 1730, 1500, 1230 and 830; δ_H 2.85 + 3.22 (*AB*X, J_{gem} 15.2, J_{vic} 2.4 and 5.2, 3-H_2), 3.30 + 3.68 (*AB*X, J_{gem} 10.2, J_{vic} 8.7 and 2.9, CH_2I), 3.79 (s, OMe), 4.11 (m, 4-H) and 6.90 + 7.29 (AA′BB′, J 9.0, 4 × ArH).

(±)-4-*Cyanomethyl*-1-(4-*methoxyphenyl*)*azetidin*-2-*one* **30a**.—A mixture of compound **33** (22 g, 66 mmol), sodium cyanide (6.5 g, 132 mmol), and DMF (70 cm^3) was stirred for 6 h at ambient temperature and poured into brine (250 cm^3). The resulting suspension was extracted with ethyl acetate (3 × 100 cm^3 + 2 × 50 cm^3). The combined organic phases were washed with water (3 × 100 cm^3), dried ($MgSO_4$), and evaporated to dryness at reduced pressure. The resulting black oil was worked up by column chromatography (ethyl acetate–hexane, 1:1) to give the title compound (8.9 g, 62%), m.p. 83–85 °C (from ethyl acetate–hexane, 1:1), R_f 0.42 (ethyl acetate–hexane, 2:1) (Found C, 66.6; H, 5.75; N, 12.7. $C_{12}H_{12}N_2O_2$ requires C, 66.65; H, 5.60; N, 12.96%) ν_{max}(KBr)/cm^{-1} 2280/2270 (d), 1760, 1510 and 830; δ_H 2.80 + 2.93 (*AB*X, J_{gem} 17.0, J_{vic} 6.0 and 4.2, CH_2CN), 2.99 + 3.32 (*AB*X, J_{gem} 15.2, J_{vic} 2.5 and 5.2, 3-H_2), 3.79 (s, OMe), 4.29 (m, 4-H) and 6.90 + 7.28 (AA′BB′, J 9.0, 4 × ArH).

(±)-1-(4-*Methoxyphenyl*)-4-(*tetrazol*-5-*ylmethyl*)*azetidin*-2-*one* **7**.—(a) A mixture of compound **30a** (5.3 g, 24.5 mmol), sodium azide (4.8 g, 74 mmol), triethylammonium chloride (5.0 g, 36.7 mmol) and *N*-methylpyrrolidin-2-one (200 cm^3) was stirred for 7 h under nitrogen at 150–155 °C (bath temperature), concentrated to *ca.* 60 cm^3 at reduced pressure, and poured into brine (300 cm^3). The resulting suspension was acidified with conc. HCl (pH 1) and extracted with ethyl acetate (3 × 100 + 2 × 50 cm^3). The combined ethyl acetate solutions were washed with brine (50 cm^3), dried ($MgSO_4$) and evaporated at reduced pressure to give an oil which crystallized when triturated with acetone to give the title compound (3.2 g, 55%), m.p. 152–156 °C, R_f 0.47 (CH_2Cl_2–methanol, 8:2) (Found: C, 55.65; H, 5.35; N, 27.05. $C_{12}H_{13}N_5O_2$ requires C, 55.59; H, 5.05; N, 27.02%) ν_{max}(KBr)/cm^{-1} 3100–2500, 1720 and 820; δ_H(CD-Cl_3 + [$^2H_6$]DMSO) 2.98 + 3.23 (*AB*X, J_{gem} 15.0, J_{vic} 2.5 and 5.3, 3-H_2), 3.21 + 3.65 (*AB*X, J_{gem} 15.0, J_{vic} 8.8 and 4.0, 4-CH_2), 3.79 (s, MeO), 4.50 (dddd, J 2.5, 5.3, 8.8 and 4.0, 4-H), 6.88 + 7.31 (AA′BB′, J 9.0, 4 × ArH) and 9.3 (br s, NH).

(b) A mixture of freshly sublimed $AlCl_3$ (6.2 g, 46 mmol) and anhydrous THF (250 cm^3) was stirred for 10 min. Sodium azide (13.5 g, 208 mmol) and, after an interval of 10 min, compound **30a** (10 g, 46 mmol) were added with continuous stirring. The mixture was refluxed for 24 h under nitrogen, allowed to cool, diluted with water (100 cm^3) and acidified to pH 1 with conc. hydrochloric acid. The resulting emulsion was extracted with EtOAc (3 × 50 cm^3). Conventional work-up of the combined organic phases afforded compound **7** (9.9 g, 82%), identical (IR) with the sample obtained as described in (a).

(±)-1-(2,4-*Dimethoxybenzyl*)-4-(*tetrazol*-5-*ylmethyl*)-*azetidin*-2-*one* **14**.—A mixture of compound **30b**[14] (11.8 g, 45 mmol), sodium azide (9.4 g, 145 mmol), triethylammonium chloride (9.7 g, 71 mmol), and *N*-methylpyrrolidin-2-one (450 cm^3) was stirred for 3 h under nitrogen at 150 °C (bath temperature) and concentrated to 80 cm^3 at reduced pressure. Water (100 cm^3) was added and the mixture was extracted with CH_2Cl_2 (4 × 50 cm^3). The aqueous phase was acidified with conc. HCl (pH 1) and extracted with ethyl acetate (5 × 50 cm^3). The combined ethyl acetate solutions were dried ($MgSO_4$) and evaporated to dryness to give the title compound (7.4 g, 54%) as an oil, R_f 0.55 (CH_2Cl_2–methanol, 8:2) (Found: C, 52.35; H, 5.35; N, 21.3. $C_{14}H_{17}N_5O_3$ requires C, 52.33; H, 5.81; N, 21.80%); ν_{max}(film)/cm^{-1} 3200–2700 and 1730; δ_H 2.6–3.6 (m, 3-H_2 + 4-CH_2), 3.80 + 3.83 (2 × s, 2 × MeO), 3.90 (m, 4-H), 4.23 + 4.49 (AB, J_{gem} 14.5, N–CH_2Ar), 6.35 + 6.5 (2 × m, 3-H + 5-H, aryl), 7.1 (d, J 8.8, 6-H, aryl) and 8.7 (br s, NH).

1-(4-*Methoxyphenyl*)-4-(2-*methyltetrazol*-5-*ylmethyl*)- **15a** *and* -4-(1-*methyltetrazol*-5-*yl*-*methyl*)-*azetidin*-2-*one* **17a**.—A freshly prepared ethereal (12 cm^3) diazomethane (0.3 g, 7.1 mmol) solution was added to a solution of compound **7** (1.0 g, 3.9 mmol) in anhydrous dioxane (50 cm^3). The mixture was

stirred at room temperature until, according to TLC (CH_2Cl_2–acetone, 7:1), compound **7** was consumed (~4 h), when it was evaporated to dryness at reduced pressure. The residue was worked up by column chromatography (CH_2Cl_2–diethyl ether, 10:1) to afford first compound **15a** (856 mg, 81%) and then compound **17a** (184 mg, 18%).

Compound **15a**: m.p. 95–97 °C (Found: C, 57.35; H, 5.6; N, 25.45. $C_{13}H_{15}N_5O_2$ requires C, 57.1; H, 5.5; N, 25.6%) ν_{max}/cm^{-1} 1730; δ_H 2.95 + 3.20 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, 3-H_2), 3.16 + 3.62 (*ABX*, J_{gem} 15.0, J_{vic} 8.5 and 3.8, 4-CH_2), 3.80 (s, OMe), 4.31 (s, *N*-Me), 4.45 (m, 4-H) and 6.90 + 7.35 (AA′BB′, 4-methoxyphenyl, ArH).

Compound **17a**: m.p. 200–202 °C (Found: C, 56.95; H, 5.4; N, 25.75. $C_{13}H_{15}N_5O_2$ requires C, 57.1; H, 5.5; N, 25.6%) ν_{max}/cm^{-1} 1730; δ_H($CDCl_3$ + [$^2H_6$]DMSO; 400 MHz) 2.95 + 3.30 (*ABX*, J_{gem} 14.8, J_{vic} 2.5 and 5.0, 3-H_2), 3.26 + 3.62 (*ABX*, J_{gem} 15.5, J_{vic} 8.5 and 3.8, 4-CH_2), 3.75 (s, OMe), 3.90 (s, *N*-Me), 4.62 (m, 4-H) and 6.90 + 7.30 (AA′BB′, 4-methoxyphenyl group, ArH).

4-[2-(*Diphenylmethyl*)*tetrazol*-5-*ylmethyl*]- **15b** *and* 4-[1-(*diphenylmethyl*)*tetrazol*-5-*ylmethyl*]-1-(4-*methoxyphenyl*)*azetidin*-2-*one* **17b**.—A mixture of compound **7** (1.0 g, 3.9 mmol), anhydrous dioxane (100 cm^3) and diphenyldiazomethane (1.5 g, 7.7 mmol) was stirred at ambient temperature until, according to TLC (CH_2Cl_2–acetone, 7:1), compound **7** was consumed (~1 week), when it was evaporated to dryness at reduced pressure. The residue was worked up by column chromatography (CH_2Cl_2–diethyl ether, 10:1) to afford first compound **15b** (1.3 g, 79%) and then compound **17b** (328 mg, 20%) as oils.

Compound **15b** (Found: C, 70.0; H, 5.3; N, 16.6. $C_{25}H_{23}N_5O_2$ requires C, 70.6; H, 5.4; N, 16.45%) ν_{max}(film)/cm^{-1} 1740; δ_H(400 MHz) 2.98 + 3.20 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, 3-H_2), 3.21 + 3.64 (*ABX*, J_{gem} 15.0, J_{vic} 8.5 and 3.8, 4-CH_2), 3.77 (s, OMe), 4.41 (m, 4-H), 6.83 + 7.26 (AA′BB′, 4-methoxyphenyl, ArH), 7.24 (s, Ph_2CH) and 7.15–7.4 m (2 × Ph).

Compound **17b** (Found: C, 70.7; H, 5.6; N, 16.3. $C_{25}H_{23}N_5O_2$ requires C, 70.6; H, 5.4; N, 16.45%) ν_{max}(film)/cm^{-1} 1740; δ_H(400 MHz) 2.78 + 3.31 (*ABX*, J_{gem} 15.3, J_{vic} 2.5 and 5.3, 3-H_2), 3.00 + 3.43 (*ABX*, J_{gem} 15.6, J_{vic} 8.2 and 4.2, 4-CH_2), 3.77 (s, OMe), 4.52 (m, 4-H), 6.66 (s, Ph_2CH), 6.83 + 7.12 (AA′BB′, 4-methoxyphenyl, ArH) and 7.0–7.4 (m, 2 × Ph).

4-(2-*Benzyltetrazol*-5-*ylmethyl*)-**15c** *and* 4-(1-*Benzyltetrazol*-5-*ylmethyl*)-1-(4-*methoxyphenyl*)*azetidin*-2-*one* **17c**.—A 1% ethanolic (6.1 cm^3) sodium ethoxide solution (2.65 mmol) and benzyl iodide (0.58 g, 2.68 mmol) were successively added to an ethanolic solution (20 cm^3) of compound **7** (0.69 g, 2.65 mmol). The mixture was heated under reflux until, according to TLC (CH_2Cl_2–acetone, 7:1), compound **7** was consumed (16 h), when it was evaporated to dryness at reduced pressure and worked up by column chromatography (CH_2Cl_2–diethyl ether, 10:1) to afford first compound **15c** (407 mg, 44%) and then compound **17c** (324 mg, 35%) as oils.

Compound **15c** (Found: C, 66.5; H, 5.3; N, 19.9. $C_{19}H_{19}N_5O_2$ requires C, 65.35; H, 5.45; N, 20.05%) ν_{max}(film)/cm^{-1} 1740; δ_H 2.93 + 3.20 (*ABX*, J_{gem} 15.0, J_{vic} 2.5 and 5.0, 3-H_2), 3.15 + 3.60 (*ABX*, J_{gem} 15.0, J_{vic} 8.5 and 3.8, 4-CH_2), 3.77 (s, OMe), 4.41 (m, 4-H), 5.7 (s, PhCH_2), 6.85 + 7.28 (AA′BB′, 4-methoxyphenyl, ArH) and 7.35 (m, Ph).

Compound **17c** (Found: C, 65.3; H, 5.7; N, 19.7. $C_{19}H_{19}N_5O_2$ requires C, 65.35; H, 5.45; N, 20.05%) ν_{max}/cm^{-1} 1740; δ_H 2.79 + 3.26 (*ABX*, J_{gem} 15.4, J_{vic} 2.5 and 5.3, 3-H_2), 3.02 + 3.37 (*ABX*, J_{gem} 15.5, J_{vic} 8.0 and 4.5, 4-CH_2), 3.80 (s, OMe), 4.47 (m, 4-H), 5.38 + 5.40 (AB, J_{gem} 15, PhCH_2), 6.85 + 7.14 (AA′BB′, 4-methoxyphenyl, ArH) and 7.0–7.45 (m, Ph).

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